Consideration of the causes of variability and appropriate statistical analyses to generate unbiased estimators and reliable confidence intervals remains a challenge for these studies.

PRM28
WHAT ARE INDIRECT COSTS IN NEURODEGENERATIVE DISEASES? A METHODOLOGICAL REVIEW
Costa N, Deruemaux-Burel H, Molinier L
University Hospital of Toulouse, Toulouse, France
OBJECTIVES: Neurodegenerative diseases (NDs) refer to a group of diseases that affect brain cells. Alzheimer disease (AD), Parkinson disease (PD), Amyotrophique Lateral Sclerosis (ALS) and Multiple Sclerosis (MS) are the most prevalent NDs. NDs cause a substantial economic burden worldwide and indirect costs are an important component of total costs. This study aims to review relevant papers to characterize the different components of indirect costs and to identify the weight of indirect costs on total costs in different NDs. **METHODS:** A systematic bibliographic search was performed on an international medical literature database (MEDLINE). All studies which assessed the social economic burden and indirect costs of different NDs were selected. Indirect costs were characterized into several types (i.e. sick leave, presenteeism, early retirement, premature death, reduction in working hours, informal care time) and into several valuation (i.e. Human Capital Approach, Friction Cost Method, Willingness To Pay). **RESULTS:** 44 studies met our criteria. Depending on studies, the percentage of indirect costs on total costs varies from 1% to 68% in PD, from 2% to 89% in AD, from 24% to 59% in ALS and from 29% to 78% in MS. The main indirect costs component was early retirement in PD, ALS and MS. This component varies from 61% to 95% of indirect costs in PD, from 35% to 88% in ALS and from 61% to 95% in MS. The main indirect costs component in AD was informal care time and account for almost 100% of indirect costs. Indirect costs increase with severity level in AD and MS, and decrease with severity level in ALS. **CONCLUSIONS:** Components of indirect costs are different depending on studies and especially for AD where indirect costs mainly refer to informal costs which should be considered as a full cost category to avoid the lack of understanding.

PRM29
NOT AS EASY AS IT SOUNDS: CHALLENGES IN ASSESSING THE VALUE FOR MONEY OF IMPLEMENTED VACCINATION PROGRAMS
Newall AT[1], Reyes J[1], Wood JG[1], McIntyre PB[2], Menzies R[2], Beutels P[3]
[1]*University of New South Wales, Sydney, Australia,* [2]*National Centre for Immunisation Research and Surveillance (NCIRS), Sydney, Australia,* [3]*University of Antwerp, Antwerp, Belgium*
OBJECTIVES: In this study we explore the methodological challenges presented by retrospective economic analyses of vaccination programs and offer direction for future evaluations in the area. Post-implementation evaluation should be an important part of assessing the success of public health programs; however relatively little attention has been focused on evaluating the value for money achieved by vaccination programs after they have been introduced. **METHODS:** We conducted a narrative review of the limited existing economic evaluation literature assessing the cost-effectiveness of implemented vaccination programs. We evaluated the alternative approaches to addressing the challenges that these retrospective evaluations present. These challenges were then contrasted and compared with those that prospective economic evaluations face. **RESULTS:** The key challenges identified for retrospective economic evaluations include the estimation of: disease changes attributable to vaccination efforts, the hypothetical no vaccination comparator scenario and the full benefits likely to be achieved by implemented vaccination programs. We also present other important factors that may need to be considered such as the evolution of prices over time. **CONCLUSIONS:** Retrospective economic analyses of vaccination programs are likely to become more frequent and influential and it is important that both the benefits and the limitations of these evaluations are recognised and understood. Further work needs to be done to explore how the practical application of alternative approaches may impact on the results of evaluations in different circumstances.

PRM30
ESTIMATING THE COST OF HEALTH CARE ASSOCIATED INFECTIONS CONTROLLING FOR BOTH PATIENT VARIABILITY AND TIME-DEPENDENT BIAS
Shi W[1], Greco G[1], Gelijns A[1], Blackstone E[2], Moskowitz A[1], O'Gara [3], Jeffries N[4], Bagiella E[1]
[1]*Icahn School of Medicine at Mount Sinai, New York, NY, USA,* [2]*Cleveland Clinic Foundation, Cleveland, OH, USA,* [3]*Brigham and Women's Hospital, Boston, MA, USA,* [4]*National Heart, Lung and Blood Institute, Bethesda, MD, USA*
OBJECTIVES: In the current health care environment, it is critical that we obtain better insights into the economic burden of major complications, such as health care associated infections (HAIs). Commonly used methods, however, are limited in that they provide cost and length of stay (LOS) estimates, adjusted either for patients' heterogeneity (generalized linear model (GLM)) or for the time dependency of HAIs (multistate model), but don't allow adjustment for both. We developed an approach that controls for both of these major confounders. **METHODS:** Our approach uses centered residuals from a GLM that account for important covariates. These residuals are then used in a multistate model to estimate the extra-LOS corrected for the lead time. To obtain the dollar value, the extra-days were multiplied by the average cost of a post-infection day. We applied GLM, multistate and our new approach to a prospective multicenter observational study, assessing the incidence of HAIs in cardiac surgery. Financial data were obtained from the University Health Consortium. **RESULTS:** Among 4320 patients, 119 (2.7%) developed major infections during index hospitalization. Patients developing major infection after their surgery had longer and costlier hospitalizations than patients who did not (33 days and $110,155 vs. 9 days and $31,530).The extra-cost and LOS due to HAIs were calculated using the three approaches. The new approach yields estimates ($34,632 and 13 *days*) that are intermediate between those obtained from GLM ($37,922 and 14 days) and multistate modeling ($29,304 and 11days). Results of simulations will be presented. **CONCLUSIONS:** The advantage of our approach, which combines GLM and multistate models, is that it adjusts for the two main sources of bias. Estimates obtained through this method are within the range defined by the other two approaches. We propose that this new method provides more accurate estimates of the actual economic burden of HAIs.

PRM31
PERFORMANCE COMPARISON OF DIFFERENT TYPES OF PROPENSITY SCORE MATCHING ALGORITHMS IN A STUDY OF RARE DISEASE TREATMENT COST COMPARISON USING REAL WORLD EVIDENCE
Han Y, Lodowski N
WG Consulting, New York, NY, USA
OBJECTIVES: It is well-accepted that data pre-processing and the creation of matching cohorts may provide a more balanced assessment in real world evidence analysis. The objective of this study is to show that proper selection of a propensity score matching (PSM) algorithm can significantly enhance the sensitivity of treatment cost comparison for rare diseases using claims databases. **METHODS:** Five years of retrospective inpatient commercial insurance claims data from Truven MarketScan™ were used to compare the six-month drug cost of 'Drug X' to 'Drug Y' for a rare disease, with Drug Y being the market leader. Within this study, three different types of PSM techniques were used (naïve matching, logit and recursive partitioning) to determine the impact of matching algorithms on the sensitivity of final comparison. A 2:1 matching ratio was used to take advantage of much larger patient pool for Drug Y. **RESULTS:** Without PSM, the difference in cost of the two treatments was not statistically significant, although these results show that the spending for Drug X patients is approximately $220 less than Drug Y users over a 6 month period. In the naïve matching method, the drug cost of treatment X was $234 lower than treatment Y, although the observed difference was not statistically significant. Using the logit regression algorithm, it was found that the mean cost of Drug X was approximately $368 lower than Drug Y ($p=0.028$). Lastly, with non-linear recursive partitioning PSM, the treatment cost of Drug X was $351 lower than Drug Y ($p=0.045$). **CONCLUSIONS:** The use of PSM in studies can help to remove potential confounders and produce unbiased results. Model-based PSM outperforms naïve matching in terms of enhancing analysis sensitivity. The careful selection of a matching algorithm can play a pivotal role in economic investigations for rare diseases using real world evidence.

PRM33
NON-ALCOHOLIC STEATOHEPATITIS CLINICAL DEVELOPMENT: AN OPPORTUNITY FOR NON-INVASIVE SERUM OR IMAGING BIOMARKERS FROM A COST-EFFICIENCY PERSPECTIVE
Agnese W, Suciu S, Liu S, Sood V, Cooreman M
Mitsubishi Tanabe Pharma America, Inc., Jersey city, NJ, USA
OBJECTIVES: Non-alcoholic Steatohepatitis (NASH) is the hepatic manifestation of metabolic syndrome with an increasing prevalence globally. Although there are no currently approved treatments, NASH therapeutic research and development efforts are ongoing, targeting multiple aspects of the complex disease pathways. Halting or reversing inflammation and progressive liver fibrosis are core endpoints to evaluate therapeutic efficacy. The choice of diagnostic tool may have implications on the length of study and related costs. **METHODS:** We sought to evaluate current studies on www.clinicaltrials.gov using search term 'NASH', and assess efficacy outcomes, related length of clinical programs, and research activities in relation to epidemiology. We included studies in our analysis that were: "Interventional, Phase 2, 3, or 4, known status", from Europe or North America, and NASH fibrosis and/or inflammation, not related to viral infection. We estimated current development costs, and applied alternative biomarker composite endpoints, to assess potential cost and time savings. **RESULTS:** As of January 2014, there are 199 NASH studies posted to clinicaltrials.gov, of which 54 studies met our criteria. Thirty seven of those 54 studies use histology (liver biopsy) as the primary endpoint at a mean timepoint of 58.5 weeks, compared to 18.1 weeks when non-invasive diagnostic methods (serum markers of inflammation and fibrosis, imaging) are used ($p<0.0001$). **CONCLUSIONS:** Our data show that utilization of non-invasive markers as primary efficacy endpoints can allow for clinical trials of considerably shorter duration which may have an impact on cost-efficiency of clinical development programs for NASH. Further study is required to expand upon these findings as well as validate biomarkers for acceptable use in registrational trials.

RESEARCH ON METHODS – Databases & Management Methods

PRM34
ALCOHOL AND SUBSTANCE USE DISORDER COMORBIDITY MEASURES: WHO IS BEING COUNTED?
Montejano LB
Truven Health Analytics, Cambridge, MA, USA
OBJECTIVES: Patients with comorbid alcohol use disorders (AUD) and substance use disorders (SUD) may be identified in administrative claims data using a range of codes (eg ICD-9 303-305), but it is not clear this yields a homogenous group. The objective of this study was to characterize patients with AUD/SUD claims to better understand the resulting comorbidity measures. **METHODS:** Patients with ≥1 claim indicative of AUD/SUD between 2005-2012 were identified in the Truven Health MarketScan® Commercial and Medicare Research Databases. Continuous enrollment 6 months before and 12 months after the earliest AUD/SUD claim was required. Patients were analyzed overall, then stratified by earliest drug of abuse (alcohol, amphetamines, cannabis, cocaine, hallucinogens, sedatives, opioids) for bivariate comparison of patient characteristics, cost and utilization. **RESULTS:** The sample included 476,628 patients; most (73%) with an AUD diagnosis. Overall, the sample was mean age 39 and 63% male. Total post-index costs were mean $17,481 and median $7,332. Other cost measures were similarly skewed. Less than half (43%) had a second AUD/SUD claim ≥30 days post-index. The sedative cohort had